Complete Summary

GUIDELINE TITLE

Acute myelogenous leukemia.

BIBLIOGRAPHIC SOURCE(S)

Acute myelogenous leukemia. Philadelphia (PA): Intracorp; 2005. Various p. [61 references]

GUIDELINE STATUS

This is the current release of the guideline.

All Intracorp guidelines are reviewed annually and updated as necessary, but no less frequently than every 2 years. This guideline is effective from April 1, 2005 to April 1, 2007.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Acute myelogenous leukemia (AML) (also called acute granulocytic leukemia, acute myeloblastic leukemia, acute myelocytic leukemia, acute myeloid leukemia, and acute nonlymphocytic leukemia) including acute promyelocytic leukemia

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Hematology
Internal Medicine
Oncology
Pediatrics

INTENDED USERS

Allied Health Personnel
Health Care Providers
Health Plans
Hospitals
Utilization Management

GUIDELINE OBJECTIVE(S)

To present recommendations for the diagnosis, treatment, and management of acute myelogenous leukemia that will assist medical management leaders to make appropriate benefit coverage determinations

TARGET POPULATION

Individuals with acute myelogenous leukemia

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Evaluation

1. Physical examination and assessment of signs and symptoms
2. Diagnostic tests:
    - Bone marrow aspiration
    - Blood work such as complete blood count, peripheral blood smear, and leukocyte alkaline phosphatase stain

Management/Treatment

1. Chemotherapy including
    - Remission induction (daunomycin and cytarabine [Ara-C] with or without 6-thioguianine or etoposide; chemotherapy and all-trans retinoic acid (ATRA) for acute promyelocytic leukemia (APL)
    - Consolidation therapy (high-dose Ara-C with or without daunomycin)
    - Maintenance therapy for children with APL (ATRA)
    - Prophylaxis and treatment of central nervous system involvement in children (intrathecal chemotherapy and craniospinal radiation)
2. Stem-cell transplantation, including
    - Allogeneic transplant
    - Autologous transplant
    - Non-myeloablative transplant
3. Physical therapy

4. Referral to specialists
5. Case management strategies, including case initiation, case management focus, and discharge

MAJOR OUTCOMES CONSIDERED

- Effectiveness of treatment
  - Remission rates
  - Survival rates
  - Rates of relapse
  - Cure rates
- Treatment-related side effects, toxicities, and complications

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Searches were performed of the following resources: reviews by independent medical technology assessment vendors (such as the Cochrane Library, HAYES); PubMed; MD Consult; the Centers for Disease Control and Prevention (CDC); the U.S. Food and Drug Administration (FDA); professional society position statements and recommended guidelines; peer reviewed medical and technology publications and journals; medical journals by specialty; National Library of Medicine; Agency for Healthcare Research and Quality; Centers for Medicare and Medicaid Services; and Federal and State Jurisdictional mandates.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Not Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not stated

METHODS USED TO ANALYZE THE EVIDENCE

Review
Review of Published Meta-Analyses

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Delphi)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

A draft Clinical Resource Tool (CRT or guideline) is prepared by a primary researcher and presented to the Medical Technology Assessment Committee or the Intracorp Guideline Quality Committee, dependent upon guideline product type.

The Medical Technology Assessment Committee is the governing body for the assessment of emerging and evolving technology. This Committee is comprised of a Medical Technology Assessment Medical Director, the Benefit and Coverage Medical Director, CIGNA Pharmacy, physicians from across the enterprise, the Clinical Resource Unit staff, Legal Department, Operations, and Quality. The Intracorp Guideline Quality Committee is similarly staffed by Senior and Associate Disability Medical Directors.

Revisions are suggested and considered. A vote is taken for acceptance or denial of the CRT.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Comparison with Guidelines from Other Groups
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Diagnostic Confirmation

Subjective Findings

- Easy/excessive bruising
- Lassitude
- Complaint of bone pain
- Minor skin irritations
- Weakness
- Report of shortness of breath
- Nervous system complaints

Objective Findings

- Fever
- May present acutely ill with notable malaise and fatigue
- Pallor, ecchymoses, and skin rashes
- Unexplained weight loss
- Splenomegaly
- Anemia
- Shortness of breath (SOB), dyspnea on exertion (DOE)
- Nosebleeds, thrombocytopenia with bleeding from mucous membranes, bruising, and petechiae, or disseminated intravascular coagulation (DIC) crisis
- Peripheral cytopenia or pancytopenia
- Bone marrow infiltration of >30% blast cells with marrow failure
- Repeated infections, such as minor skin or systemic infections
- Central nervous system involvement (rare)
- Visible tissue or nervous system infiltration (rare)

Diagnostic Tests

- Bone marrow aspiration
    - Myeloblast cells >30% of nucleated marrow cells confirms acute myelogenous leukemia (AML) diagnosis.
- Blood work that may be ordered:
    - Complete blood count (CBC)
        - Critical values: hemoglobin (Hgb) <9 gm/dL; hematocrit (Hct) <25 volume %; platelets (Plts) < 30,000/mm^3.
        - High white blood cell (WBC) at presentation is a significant prognostic indicator of early mortality.
        - AML causes increased granulocytes, decreased red blood cells (RBCs), and decreased platelets (thrombocytopenia, platelets < 100,000/mm^3).
        - Responding to later stages of inflammation, inadequate eosinophil numbers (agranulocytosis) indicate an extremely poor prognosis and often fatal outcome.
    - Peripheral blood smear
        - Immature white blood cells (WBCs) ("pro-lymphocytes") in high numbers indicate leukemia.
    - Leukocyte alkaline phosphatase (LAP) stain
        - Normal findings: 30 to 130 LAP units
        - AML can be distinguished from temporary leukocytosis by LAP stain values. Patients with untreated AML have LAP values <20:

leukocytosis caused by infection or steroid use produces high LAP values.

Differential Diagnosis

- "Pseudoleukemia" during recovery from drug-induced or Pseudomonas-induced agranulocytosis
- Primary bone marrow failure (aplastic anemia)
- Leukemoid reaction (can be distinguished by LAP score)

Treatment Options

Chemotherapy

Treatment of AML is divided into two phases: induction and intensification. Induction treatment uses a combination of drugs, most commonly daunomycin and cytarabine (Ara-C), with or without 6-thioguianine. High-risk patients may also be treated with etoposide. Treatment is repeated every four weeks until complete remission (CR), which the National Cancer Institute (NCI) has defined as including all of the following:

- Peripheral-blood counts rising toward normal
- A mildly hypocellular to normal cellular marrow with fewer than 5% blasts
- No clinical signs or symptoms of the disease, including in the central nervous system (CNS) or at other extramedullary sites

Treatment for acute promyelocytic leukemia (APL) includes chemotherapy as well as all-trans retinoic acid (ATRA). Children with Down syndrome fare better with less intense therapy (lower doses and longer periods between treatments); they also benefit from chemotherapy intensification rather than bone-marrow transplant.

Intensification (or consolidation) therapy begins in CR. The most common therapy is high-dose cytarabine, with or without daunomycin. Generally, one or two courses are given, sometimes followed by allogeneic stem-cell transplantation. In children, intrathecal chemotherapy is usually given every one to two months for as long as intensification continues.

Maintenance therapy is not needed for adults and children with AML. Children with APL are the exception; they may continue to receive ATRA for about one year.

Because refractory and recurrent AML have such poor prognoses, most children with these diagnoses are entered into clinical trials. If these children achieve remission, allogeneic stem-cell transplantation should be considered. The cure rate with standard chemotherapy is 40 to 50%; with hematopoietic stem-cell (HSC) transplantation, the cure rate is 55 to 60%.

CNS prophylaxis is not indicated in adults, because only 5% of adult AML patients develop CNS involvement. APL is generally not treated with prophylactic intrathecal chemotherapy, as this type of leukemia rarely presents with CNS involvement, and intrathecal chemotherapy increases the risk of severe bleeding.

In children, CNS prophylaxis consists of intrathecal chemotherapy without radiation. Although this therapy has not been proven to improve overall survival among children with AML, isolated CNS disease has been found among approximately 20% of children who receive no CNS prophylaxis. For this reason, most regimens for children include this treatment. Treatment of CNS involvement in children may include craniospinal radiation, in addition to intrathecal chemotherapy.

Stem Cell Transplant

Stem-cell transplantation refers to transplantation of hematopoietic stem cells (HSCs) from a donor into a patient. HSCs are immature cells that can develop into any of the three types of blood cells (red cells, white cells, or platelets). HSC transplantation can be either autologous (using the patient's own stem cells) or allogeneic (using stem cells from a donor). HSC transplantation is provided to patients with hematological malignancies to rescue the patients from treatment-induced aplasia, after high-dose chemotherapy and/or radiotherapy has been administered to eliminate the cancer. Many factors affect the outcome of a tissue transplant. The patient selection process is designed to obtain the best result for each patient.

Allogeneic Transplant

Allogeneic stem-cell transplantation involves using HSCs from a donor. In order for such a transplant to be successful, the donated cells must be similar, or a match, to the recipient's. Human leukocyte antigen (HLA) typing can identify donors who may be a perfect match. HLAs are proteins on the surface of cells. These proteins help the immune system identify a cell as either belonging to the body or from outside the body. There are three types each of class I and class II HLA. Increased survival is associated with a match between recipient and donor HLA-A, HLA-B, HLA-C, HLA-DRB1, and HLA-DQB1.

Autologous Transplant

Autologous HSC transplantation is the transplantation of the recipient's own previously harvested stem cells. Autologous HSC transplant provides an alternative stem-cell source for patients who do not have an HLA-identical donor. It can also be performed in older patients, since the conditioning regimen for autologous transplantation is less toxic than the one for allogeneic HSC transplantation and does not create a graft-versus-host reaction. However, this lack of graft-versus-leukemia reaction with autologous HSC transplantation results in greater chances of disease relapse compared to the chances with allogeneic HSC transplantation. Contamination of autografts by malignant cells may account for the difference.

Non-Myeloablative Transplant

Non-myeloablative preparative regimens (also called mini-transplants) are designed to reduce regimen-related toxicities and allow allogeneic transplantation in patients who are older, have comorbid conditions or have toxicities from previous treatment. Non-myeloablative conditioning regimens fall into two categories: reduced intensity and minimally myelosuppressive. Conditioning

regimen varies by study protocol and may include a purine analog, an alkylating agent, or low-dose total-body irradiation. The purine analogs (including fludarabine, cladribine, and pentostatin) are broadly cytotoxic, as well as immunosuppressive.

Source of Cells

HSCs are available in the peripheral blood, bone marrow, and umbilical cord.

Refer to related guideline for additional background and medical necessity information on stem cell transplantation for AML.

Duration of Medical Treatment

- Medical - Optimal: 120 day(s), Maximal: 720 day(s)
    - Acute: Induction and consolidation phases may each last 4 to 8 weeks, depending on severity and persistence of complications and side effects of therapy.
    - Although a significant percentage of patients achieve initial remission, relapses are frequent. Second remissions are more difficult to achieve and disability may be severe and lengthy.
    - Maintenance therapy: Usually lasts about 2 years; this may be extended through patient's lifetime

Additional information regarding primary care visit schedules, referral options, specialty care, and physical therapy is provided in the original guideline document.

The original guideline document also provides a list of red flags that may affect disability duration, and return to work goals, including

- After chemotherapy, first remission
- After relapse and second remission
- After HSC transplant
- On-going illness without remission

Note: Some patients with this condition may never return to work.

Case Management Directives (refer to the original guideline for detailed recommendations)

Case Initiation

Establish Case

- Document baseline information, history, key physical findings, patient's understanding, and safety factors.
- Refer to Chemotherapy Chart in the original guideline document.
- The American Joint Committee on Cancer encourages use of the "TNM" classification system (T=primary tumor size; N=lymph node involvement; M=metastasis).

- Provide contact information for local and national support groups.

Coordinate Care

- Advocate for patient by managing utilization and charges.
- Document treatment plan.

Case Management Focus

Activity Deficit

- Document activity alteration as none, mild, moderate, severe, dependent, or bed-bound (based on most recent performance status) and interventions required.

Chemotherapy Intolerance

- Assess status, acute versus chronic, of toxic side effects on rapidly growing tissues, including bone marrow, epithelium, hair, sperm, and document intervention recommended.

Hemodynamic Instability

- Document bleeding complications, severity, and intervention recommended.

Immune Compromised

- Document establishment of protective isolation measures for a white blood cells count (WBC) less than 1,000/mm^3, implying dangerous susceptibly to infection.

Inadequate Nutrition

- Use optimal goal of remaining within 10% of pretreatment weight to document hydration and nutrition deficit as mild, moderate, severe, and response needed.

Mental and Emotional Alteration

- Ensure accurate diagnosis of any change in mental status.
- Document baseline or optimal mental and emotional functioning and their alterations due to cancer presence, comorbidity, surgery, or treatments.
- Assess and respond appropriately to the degree of debility caused by alterations listed in the original guideline document through benefit coordination or community resource activation.

Pain Control

- Document optimal pain management by characterizing severity and interventions undertaken to remedy or manage pain.

Oncologic Emergencies

- Document presence of or developing oncologic emergencies and report to attending physician, surgeon, or activate emergency medical technician (EMT) system as necessary.

Radiation Intolerance

- Document presence and severity of radiation side effects.
- Initiate early interventions for complications of radiation therapy.

Respiratory Instability

- Document respiratory deficit as mild, moderate, severe, and dependent, and respiratory rehabilitation enhancement measures.

Skin Integrity Deficit

- Document severity of skin integrity disruption.

Terminal Care

- Document optimal comfort measures and palliative care initiatives.

Discharge

Discharge from Case Management (CM)

- Document return to independence or stabilized functional status and closing conversations with patient, caregiver, physician, pharmacist, and care providers.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

General Potential Benefits

Appropriate diagnosis, treatment, and management of acute myelogenous leukemia that assist medical management leaders in making appropriate benefit coverage determinations

Specific Benefits

- The conditioning regimen for autologous transplantation is less toxic than the one for allogeneic hematopoietic stem cells (HSC) transplantation and does not create a graft-versus-host reaction.
- With treatment, 60 to 70% of adult patients with acute myelogenous leukemia (AML) achieve complete remission; children achieve 75 to 85% complete remission.
- The cure rate with standard chemotherapy is 40 to 50% for children with refractory and recurrent AML who have achieved remission; with HSC transplantation, the cure rate is 55 to 60%.

POTENTIAL HARMS

Refer to the Case Management Focus section of the "Major Recommendations" field for information on potential complications and strategies to address them, or refer to the original guideline document.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Acute myelogenous leukemia. Philadelphia (PA): Intracorp; 2005. Various p. [61 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1997 (revised 2005)

GUIDELINE DEVELOPER(S)

Intracorp - Public For Profit Organization

SOURCE(S) OF FUNDING

Intracorp

GUIDELINE COMMITTEE

CIGNA Clinical Resources Unit (CRU)
Intracorp Disability Clinical Advisory Team (DCAT)
Medical Technology Assessment Committee (MTAC)
Intracorp Guideline Quality Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Not stated

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

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GUIDELINE AVAILABILITY

Electronic copies: Intracorp guidelines are available for a licensing fee via a password protected, secure Web site at www.intracorp.com.

Reprints of complete guideline content may be purchased for $35.00 per title (plus tax in TX at 8.25% and CT at 1.0%). Please send e-mail request to lbowman@mail.intracorp.com.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Policies and procedures. Medical Technology Assessment Committee Review Process. Philadelphia (PA): Intracorp; 2004. 4 p.
- Online guideline user trial. Register for Claims Toolbox access at www.intracorp.com.

Licensing information and pricing: Available from Intracorp, 1601 Chestnut Street, TL-09C, Philadelphia, PA 19192; e-mail: lbowman@mail.intracorp.com.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on May 24, 2005. The information was verified by the guideline developer on June 7, 2005.

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DISCLAIMER

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